

REMARKS

Claims 1-64 are pending. Claims 1-18 and 37-64 have been cancelled without prejudice to the filing of a divisional application thereon.

I. Objections to the Drawings Have Been Addressed

Applicants have amended Figure 2 to include the legend – Prior Art –. Applicants respectfully request that the objection to the Drawings be withdrawn.

II. Objections to the Abstract Have Been Addressed

Applicants have replaced the abstract with the substitute abstract appearing on the page 15 of this Amendment. Applicants respectfully request that the objection to the Abstract be withdrawn.

III. Claims 19 and 20 Are Definite

Claims 19-36 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Referring to claim 19, the Action states that “[i]t is not clear, what is meant by ‘a filter line . . . communicating with a filter medium.’ If the filter line does not comprise the filter medium, then it is not clear, why it is called the ‘filter line.’ Moreover, the specification unambiguously discloses: ‘a filter medium is disposed in the filter line.’” Referring to claim 20, the Actions states that it is not clear what type of needle is meant here, as needles can be solid. Applicants respectfully traverse these rejections.

Claim 19 has been amended to recite “a filter medium disposed in or at an end of the filter line.” Support for this amendment can be found, for example, at page 12, which states “A filter medium F may be installed anywhere along filter line FL in communication with filter tubing 88, but preferably is integrated into second port 82 of first valve V1” and in Figure 4. Applicants respectfully request that this rejection be withdrawn.

Claim 20 has been amended to recite “wherein the sampling means is a needle having a channel through which fluid can pass.” Support for this amendment can be found, for example, at page 18, which describes “[t]he fluid conduits of workstation CW, including sample needle SN, are flushed using a solvent such as acetonitrile

supplied from the needle rinse reservoir 95.” Applicants respectfully request that this rejection be withdrawn.

IV. Claims 19-20 and 25-36 Are Patentable Over PADA in view of Blake-Coleman

Claims 19-20 and 25-36 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over the Prior Art Disclosed by Applicants in Figure 1 (PADA) in view of U.S. Patent No. 4,848,139 to Blake-Coleman, et al. (Blake-Coleman). Applicants respectfully traverse this rejection.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure.¹ M.P.E.P. § 2142. Applicant respectfully submits that the Patent Office has not established a *prima facie* case of obviousness for at least the reason that there is no motivation to combine PADA with Blake Coleman to arrive at the invention recited in claim 19.

Blake-Coleman is directed to methods and apparatus for determining the number of bacteria contained in a fluid medium. Blake-Coleman does not provide motivation for combining a portion of the apparatus for determining the number of bacteria contained in a fluid medium of Blake-Coleman with a liquid sampling device as shown in prior art Figure 1 of the present application to obtain a crystal form screening workstation, as recited in claim 19. Moreover, prior art Figures 1 and 2 provide no motivation to combine the illustrated liquid handling systems with the

¹ Because all three criteria must be met in order to establish a *prima facie* case of obviousness, and the criterion that there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings has not been met, Applicants address this criterion without discussion of the other two criteria, namely whether the prior art references when combined teach or suggest all the claim limitations and whether there is a reasonable expectation of success. Applicants' decision not to discuss these other two criteria is in no way an acquiescence that these criteria have been proven by the Patent Office, and Applicants expressly reserve the right to address one or both of these criteria in future responses, should the need arise.

apparatus for determining the amount of biological material in a system proposed by Blake-Coleman to arrive at the invention recited in claim 19. Claims 20 and 25-36 each depend from patentable independent claim 19. For at least this reason and without acquiescing in the Action's rejections of these claims, Applicants respectfully submit that these dependent claims are also patentable. Applicants expressly reserve the right to argue the separate patentability of one or more of these dependent claims at a future time.

For at least the foregoing reasons, Applicants respectfully submit that claims 19-20 and 25-36 are patentable over PADA in view of Blake-Coleman and request that these rejections be withdrawn.

V. Claims 21-23 Are Patentable Over PADA in view of Blake-Coleman and further in view of Messing

Claims 21-23 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over the Prior Art Disclosed by Applicants in Figure 1 (PADA) in view of Blake-Coleman and further in view of U.S. Patent No. 3,930,951 to Messing (Messing). Claims 21-23 each depend from patentable independent claim 19. For at least this reason and without acquiescing in the Action's rejections of these claims, Applicants respectfully submit that these dependent claims are also patentable and request that these rejections be withdrawn. Applicants expressly reserve the right to argue the separate patentability of one or more of these dependent claims at a future time.

VI. Claim 24 Is Patentable Over PADA in view of Blake-Coleman and Messing and further in view of Dorsey

Claim 24 has been rejected under 35 U.S.C. § 103(a) as being unpatentable over the Prior Art Disclosed by Applicants in Figure 1 (PADA) in view of Blake-Coleman and Messing and further in view of U.S. Patent No. 4,919,804 to Dorsey (Dorsey). Claim 24 depends from patentable independent claim 19. For at least this reason and without acquiescing in the Action's rejections of this claim, Applicants respectfully submit that this dependent claim is also patentable and request that this rejection be withdrawn. Applicants expressly reserve the right to argue the separate patentability of this dependent claim at a future time.

VII. Claims 19-20 and 25-36 Are Patentable Over Kenyon in view of SPSS and Blake-Coleman

Claims 19-20 and 25-36 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over the WO 93/07311 (Kenyon) in view of “the Standard Protocol for Screening Solid (SPSS) disclosed by Applicants at page 2” (the Action, page 5) and Blake-Coleman. The Action states that “[i]t would have been obvious for anyone of ordinary skill in the art to modify Kenyon’s apparatus by including means for dissolving solids and filtering resultant solutions before crystallizing, because SPSS discloses these steps as conventional for screening crystal forms, and Kenyon’s apparatus is applied for screening crystal forms of drugs, with the latter usually present as solid formulations.” (The Action, page 5). Applicants respectfully traverse this rejection.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure.² M.P.E.P. § 2142. Applicant respectfully submits that the Patent Office has not established a *prima facie* case of obviousness for at least the reason that there is no motivation to combine Kenyon with “SPSS” and Blake-Coleman to arrive at the invention recited in claim 19.

Kenyon is directed to a device for forming crystals by vapor diffusion in the hanging drop method. As described by Kenyon at page 58, line 25, to page 64, line

² Because all three criteria must be met in order to establish a *prima facie* case of obviousness, and the criterion that there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings has not been met, Applicants address this criterion without discussion of the other two criteria, namely whether the prior art references when combined teach or suggest all the claim limitations and whether there is a reasonable expectation of success. Applicants' decision not to discuss these other two criteria is in no way an acquiescence that these criteria have been proven by the Patent Office, and Applicants expressly reserve the right to address one or both of these criteria in future responses, should the need arise.

22, the automated crystallization system (100) performs the hanging drop method by pipetting reservoir solutions containing a precipitating agent to each of the wells of a base plate, pipetting droplets containing a macromolecular solution within each circular bead of a cover, rotating the cover 180 degrees so that a droplet is suspended above each of the wells as shown in Figures 6 and 7, and sealing the cover to the plate to provide a prepared crystal forming device. The prepared crystal forming devices are then removed from the automated system and placed in the appropriate temperature environment, to promote crystallization. At page 23, lines 1-9, Kenyon describes how as each droplet hangs in a suspended state over its respective reservoir solution, the macromolecular solution in each droplet is allowed to equilibrate with the respective reservoir solution, which contains a higher concentration of the precipitating agent. Over time, water vapor diffuses from the less concentrated macromolecular solution of the droplet to the more concentrated reservoir solution and slowly increases the concentration of macromolecule and precipitating agent within each droplet.

Thus, in the hanging drop method of Kenyon, the pipette delivery system is only used to deliver solutions to the wells and droplets to the cover, not to deliver solutions to the wells and remove solutions from the wells. Accordingly, Kenyon provides no motivation to modify the apparatus of Kenyon to include “a first valve fluidly communicating with the fluid movement controller via a transfer line interposed therebetween; a second valve fluidly communicating with the sampling means; a filter line interposed between the first and second valves; a filter medium disposed in or at an end of the filter line; and a bypass line interposed between the first and second valves, wherein the first and second valves are adjustable alternately to define a first fluid conduit between the transfer line and the sampling means through the filter line and to define a second fluid conduit between the transfer line and the sampling means through the bypass line” as recited in claim 19.

Moreover, the “SPSS” as it is called by the Action provides no motivation to modify the apparatus of Kenyon to arrive at the invention recited in claim 19. As noted by the Action, page 2 of the specification describe the protocol for screening crystal forms, referred to in the Action as the Standard Protocol for Screening Solid (SPSS), which “may generally involve: (1) dissolving the drug in a solvent medium; (2) evaporating solvent, cooling the drug/solvent mixture, or adding an antisolvent to

increase the degree of supersaturation of the drug in the solvent medium and (3) characterizing the resulting products using techniques such as polarized light microscopy, thermal analysis, Raman spectroscopy, and X-ray powder diffraction.” (Specification, page 2). Contrary to the assertions of the Action, the protocol for screening crystal forms described in the specification does not describe filtering resultant solutions before crystallizing.

Furthermore, as described above in Section IV, Blake-Coleman is directed to methods and apparatus for determining the number of bacteria contained in a fluid medium. Blake Coleman does not provide any motivation for combining a portion of the apparatus for determining the number of bacteria contained in a fluid medium of Blake-Coleman with the automated hanging drop method crystallization apparatus of Kenyon to obtain a crystal form screening workstation, as recited in claim 19. Accordingly, as there is no motivation to combine Kenyon with “SPSS” and Blake-Coleman to arrive at the invention recited in claim 19, claim 19 is patentable over Kenyon in view of “SPSS” and Blake-Coleman.

Claims 20 and 25-36 each depend from patentable independent claim 19. For at least this reason and without acquiescing in the Action’s rejections of these claims, Applicants respectfully submit that these dependent claims are also patentable. Applicants expressly reserve the right to argue the separate patentability of one or more of these dependent claims at a future time.

For at least the foregoing reasons, Applicants respectfully submit that claims 19-20 and 25-36 are patentable over Kenyon in view of “SPSS” and Blake-Coleman and request that these rejections be withdrawn.

VIII. Claims 21-23 Are Patentable Over Kenyon in view of “SPSS” and Blake-Coleman and further in view of Messing

Claims 21-23 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over the Kenyon in view of “SPSS” and Blake-Coleman and further in view of Messing. Claims 21-23 each depend from patentable independent claim 19. For at least this reason and without acquiescing in the Action’s rejections of these claims, Applicants respectfully submit that these dependent claims are also patentable and request that these rejections be withdrawn. Applicants expressly reserve the right

to argue the separate patentability of one or more of these dependent claims at a future time.

IX. Claim 24 Is Patentable Over Kenyon in view of “SPSS” and Blake-Coleman and Messing and further in view of Dorsey

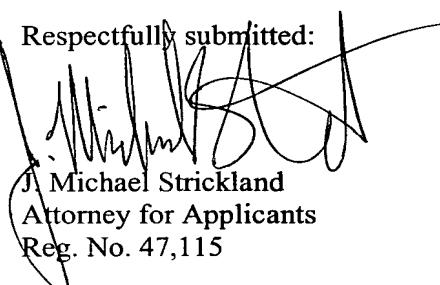
Claim 24 has been rejected under 35 U.S.C. § 103(a) as being unpatentable over Kenyon in view of “SPSS” and Blake-Coleman and Messing and further in view of Dorsey. Claim 24 depends from patentable independent claim 19. For at least this reason and without acquiescing in the Action’s rejections of this claim, Applicants respectfully submit that this dependent claim is also patentable and request that this rejection be withdrawn. Applicants expressly reserve the right to argue the separate patentability of this dependent claim at a future time.

X. Conclusion

Applicants respectfully request the withdrawal of all objections and rejections and the issuance of a Notice of Allowance forthwith.

Applicants encourage the Examiner to direct any questions regarding this application to the undersigned, who may be contacted at (919) 483-9024.

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Amendments to the Drawings:

Please substitute the enclosed Figure 2, which has been amended to include the legend – Prior Art –.